

ES against whole type 5 M protein (Dale, J.B. and Beachey, E.H., "Multiple heart-cross-reactive epitopes of streptococcal M proteins," *J. Exp. Med.* 161:113-122, 1985). —

Please replace the paragraph beginning at page 22, line 20, with the following rewritten paragraph:

E9 -- Three rabbits each were immunized with 100 µg doses of the hexavalent vaccine in either alum or CFA. Booster injections of the same dose were given at 4 and 8 weeks in either alum or saline, respectively. ELISA titers were determined using the purified hexavalent protein as the solid phase antigen (Figure 3). Sera from the animals that received the hexavalent vaccine in alum had antibody titers that were equal to or greater than the sera from rabbits that received the same dose in CFA. In a subsequent experiment, three rabbits were immunized i.m. with 100 µg of the hexavalent vaccine in saline alone according to the same schedule. None of these rabbits developed significant antibody titers against either the immunogen or the respective pep M proteins (data not shown). These data indicate that alum is a suitable and necessary adjuvant for the multivalent vaccine and is equal to the adjuvant activity of CFA in combination with the hexavalent protein. --

In the Claims:

✓ ✓ ✓ ✓ ✓ ✓ ✓ ✓ ✓ ✓ ✓ ✓ ✓ ✓
Please cancel claims 13, 14, 18, 20, 22, 24-26, 28, 29, 33, 35, 39, 41, 43, and 45-48 without prejudice to the filing of any divisional, continuation, or continuation-in-part application

Please amend claims 12, 15-17, 19, 21, 23, 27, 30, 32, 36-38, 40, 42 and 44 to read as follows:

12. (Amended) A recombinant fusion polypeptide, comprising:

(a) a multivalent immunogenic portion wherein the immunogenic portion comprises at least two immunogenic peptides, the peptides comprising at least 10 amino acids and capable of eliciting an immune response against Group A Streptococci; and

E10 (b) a C-terminal peptide which protects the immunogenicity of the immunogenic portion, wherein the C-terminal peptide is a reiteration of at least one immunogenic peptide from the amino-terminal of the immunogenic portion and is not required to stimulate an immune response against Group A Streptococci.

15. (Amended) The polypeptide according to claim 12 wherein at least one of the immunogenic peptides is from a Group A Streptococci serotype selected from the group consisting of 1, 2, 3, 4, 5, 6, 11, 12, 13, 14, 18, 19, 22, 24, 28, 30, 48, 49, 52 and 56.

E11 Sub G5 16. (Amended) The polypeptide according to claim 12 wherein the immunogenic portion consists of six immunogenic peptides, wherein the peptides are an amino-terminal portion of at least one M protein.

17. (Amended) The polypeptide according to any one of claims 12 or 15-16 wherein at least one of the immunogenic peptides is from a serotype 11 Group A Streptococci.

E12 Sub G2 19. (Amended) The polypeptide according to any one of claims 12 or 15-16 wherein at least one of the immunogenic peptides is from a serotype 13 Group A Streptococci.

E13 Sub G1 21. (Amended) The polypeptide according to any one of claims 12 or 15-16 wherein at least one of the immunogenic peptides is from a serotype 22 Group A Streptococci.

E14 Sub G8 23. (Amended) The polypeptide according to any one of claims 12 or 15-16 wherein at least one of the immunogenic peptides is from a serotype 28 Group A Streptococci.

E15 27. (Amended) A composition for promoting an immune response against Group A Streptococci, comprising:

Sub G9 (a) a recombinant fusion polypeptide, comprising:

(i) a multivalent immunogenic portion wherein the immunogenic portion comprises at least two immunogenic peptides, the peptides comprising at least 10 amino acids and capable of eliciting an immune response against Group A Streptococci; and

E15 (ii) a C-terminal peptide which protects the immunogenicity of the immunogenic portion, wherein the C-terminal peptide is a reiteration of at least one immunogenic peptide from the amino-terminal of the immunogenic portion and is not required to stimulate an immune response against Group A Streptococci; and

(b) a pharmaceutically acceptable excipient or diluent.

E16 Sub 13 30. (Amended) ~~The composition according to claim 27, further comprising an adjuvant.~~

E17 Sub 13 32. (Amended) ~~The composition according to any one of claims 27 or 30-31, further comprising an immunomodulatory cofactor.~~

Sub 601 E18 36. (Amended) The composition according to any one of claims 27 or 30-31 wherein at least one of the immunogenic peptides is from a Group A Streptococci serotype selected from the group consisting of 1, 2, 3, 4, 5, 6, 11, 12, 13, 14, 18, 19, 22, 24, 28, 30, 48, 49, 52 and 56.

37. (Amended) The composition according to any one of claims 27 or 30-31 wherein the immunogenic portion consists of six immunogenic peptides, wherein the peptides are an amino-terminal portion of at least one M protein.

38. (Amended) The composition according to any one of claims 27 or 30-31 wherein at least one of the immunogenic peptides is from a serotype 11 Group A Streptococci.

E19 Sub 601 40. (Amended) The composition according to any one of claims 27 or 30-31 wherein at least one of the immunogenic peptides is from a serotype 13 Group A Streptococci.

E20 Sub G12
42. (Amended) The composition according to any one of claims 27 or 30-31 wherein at least one of the immunogenic peptides is from a serotype 22 Group A Streptococci.

E21 Sub G13
44. (Amended) The composition according to any one of claims 27 or 30-31 wherein at least one of the immunogenic peptides is from a serotype 28 Group A Streptococci.

Please add new claims 54-58 to read as follows:

Sub G14
54. (New) The polypeptide according to any one of claims 12 or 27 wherein only one immunogenic peptide is reiterated.

E22 Sub I3
55. (New) The polypeptide according to claim 16 wherein each M protein portion is from a different Group A Streptococcal serotype, the serotypes being 1, 3, 5, 6, 19, and 24.

Sub G15
56. (New) The polypeptide according to any one of claims 12 or 27 wherein the immunogenic portion consists of ten immunogenic peptides, wherein the peptides are an amino-terminal portion of a M protein.

Sub I3
57. (New) The polypeptide according to claim 56 wherein each M protein portion is from a different Group A Streptococcal serotype, the serotypes being 1, 3, 5, 6, 18, 19, 22, 24, 28, and 30.

58. (New) The polypeptide according to any one of claims 12 or 27 wherein the immune response against Group A Streptococci comprises opsonic antibodies that do not cross-react with human tissue.

heart, kidney tissue
immune